STIC-ILL 391,819 10/4/18

From: Chen, Shin-Lin
Sent: Wednesday, April 17, 2002 7:48 PM
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Subject: articles

Please provide the following articles ASAP. Thanks!
Serial No. 09/554,996.

L4 ANSWER 10 OF 12 MEDLINE DUPLICATE 4
AU Rekhter M D; Bauman O A; Mironov A A
TI [Changes in three-dimensional structure of the internal elastic membrane of rat aorta after its mechanical injury and regeneration].
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SO ARKHIV ANATOMII, GISTOLOGII I EMBRIOLOGII, (1991 Jan) 100 (1) 14-8.

L4 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS
AU Tajima, Shingo
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SO Connect. Tissue (1997), 29(4), 235-240

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L4 ANSWER 7 OF 12 MEDLINE
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L4 ANSWER 8 OF 12 MEDLINE
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TI Minoxidil stimulates elastin expression in aortic smooth muscle cells.
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L4 ANSWER 9 OF 12 MEDLINE DUPLICATE 3
AU Rabinovitch M
TI Investigational approaches to pulmonary hypertension.
SO TOXICOLOGIC PATHOLOGY, (1991) 19 (4 Pt 1) 458-69. Ref: 58

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4/04/18

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CAS 4/19

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39/953

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SO TOXICOLOGIC PATHOLOGY, (1991) 19 (4 Pt 1) 458-69. Ref: 58

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(FILE 'HOME' ENTERED AT 19:25:33 ON 17 APR 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 19:26:01 ON 17 APR 2002

L1 9677 S ELASTINE OR TROPOELASTIN OR ELASTIC(W)FIBER
L2 103289 S INHIBIT?(6A)PROLIFERATION OR STIMULAT?(6A)DIFFERENTIATION OR
L3 22 S L1 AND L2
L4 12 DUP REM L3 (10 DUPLICATES REMOVED)

=> d 1-12 au ti so ab l4

L4 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2002 ACS
IN Wight, Thomas N.; Merrilees, Mervyn
TI Method for constructing versican V3 expressing cassette with retrovirus and therapeutic uses thereof
SO PCT Int. Appl., 108 pp.
CODEN: PIXXD2
AB The invention provides a viral vector comprising a nucleic acid sequence encoding versican V3 or a biol. active fragment or variant thereof. The invention also provides a host cell, the genome of which is augmented by a nucleic acid sequence encoding V3 or a biol. active fragment or variant thereof. The invention also provides a method to produce V3 or a biol. active fragment or variant thereof. The invention also provides a method to prevent or treat a pathol. condition in a mammal wherein V3 is implicated and an increase in V3 activity is indicated comprising administering to the mammal a therapeutically effective amt. of an agent.

L4 ANSWER 2 OF 12 MEDLINE DUPLICATE 1
AU Sugitani H; Wachi H; Tajima S; Seyama Y
TI Nitric oxide stimulates elastin expression in chick aortic smooth muscle cells.
SO BIOLOGICAL AND PHARMACEUTICAL BULLETIN, (2001 May) 24 (5) 461-4.
Journal code: BPZ; 9311984. ISSN: 0918-6158.
AB Nitric oxide (NO), an endothelium-dependent relaxing factor, **regulates** relaxation, proliferation, and **migration** of smooth muscle cells (SMCs) and most likely attenuates developing vascular disease such as atherosclerosis. We investigated whether or not NO is associated with regulation of aortic elasticity. S-Nitrosoglutathione (GSNO), a NO donor, stimulated **tropoelastin** synthesis in cultured SMCs during both the quiescent and proliferating phases. The stimulation of **tropoelastin** synthesis was dose-dependent within 1-100 nM. Maximum stimulation was detected by treatment with 100 nM GSNO for 24 h. 8-Bromoguanosine 3',5'-cyclic monophosphate (8-Br-cGMP), an exogenous cyclic GMP analog, also upregulated **tropoelastin** synthesis. **Tropoelastin** and lysyl oxidase mRNA expression, as assessed by Northern blot analysis, was also stimulated by GSNO. Administration of KT5823, a cyclic GMP-dependent protein kinase inhibitor, inhibited the GSNO-induced **tropoelastin** synthesis. These results indicate that the stimulatory effects of GSNO are due to cyclic GMP dependent protein kinase (PKG) activation by NO. In conclusion, NO seems to enhance aortic elasticity via **tropoelastin** and lysyl oxidase upregulation.

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS

IN Keating, Mark T.; Li, Dean Y.
TI Elastin-based compositions for screening of drugs for treatment of vascular diseases
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
AB The present invention provides screening methods that use organisms or cells that lack function in one or both elastin genes. These methods are useful in identifying drugs for the prevention and treatment of obstructive vascular diseases, such as atherosclerosis, vascular restenosis and transplant arteriopathy. Further, the invention provides pharmaceutical compns. contg. elastin-based compns. that are particularly potent **regulators** of proliferation, differentiation, and **migration** of smooth muscle cells in vitro and in vivo. These pharmaceutical compns. and related methods are useful in the prevention and treatment of disorders characterized by diminished capacity to regulate smooth muscle cell function.

L4 ANSWER 4 OF 12 MEDLINE DUPLICATE 2
AU Horiki S; Miyauchi-Hashimoto H; Tanaka K; Nikaido O; Horio T
TI Protective effects of sunscreening agents on photocarcinogenesis, photoaging, and DNA damage in XPA gene knockout mice.
SO ARCHIVES OF DERMATOLOGICAL RESEARCH, (2000 Oct) 292 (10) 511-8.
Journal code: 6X7. ISSN: 0340-3696.
AB We investigated the protective effects of commercial sunscreening agents against UVB-induced photoresponses in group A xeroderma pigmentosum (XPA) model mice. XPA gene-deficient mice are defective in nucleotide excision repair and show a high incidence of skin tumors and severe acute inflammation in response to UVB irradiation, in a similar manner to XP patients. SPF 10 and SPF 60 sunscreens protected partially and almost completely, respectively, ear swelling responses produced by UVB up to 200 mJ/cm2 in (-/-) mice. XPA (-/-) mice were irradiated three times a week to a cumulative dose of 2.6 J/cm2 UVB for a period of 24 weeks with or without SPF 10 or SPF 60 sunscreen. UV-induced skin tumors had developed in all unprotected (-/-) mice (13.3 tumors per mouse) at the completion of UVB irradiation. The SPF 60 sunscreen afforded stronger protection against photocarcinogenesis (1.0 tumors per mouse) than the SPF 10 sunscreen (4.4 tumors per mouse). Regarding photoaging, SPF 60 sunscreen also protected against mast cell infiltration (79% **inhibition**), **elastic fiber** accumulation, and dermal cyst **proliferation** in XPA (-/-) mice compared with unprotected (-/-) mice. In (-/-) mice, the SPF 60 sunscreen provided stronger protection against cyclobutane pyrimidine dimer formation shown immunohistologically following irradiation with 200 mJ/cm2 UVB than the SPF 10 sunscreen. The XPA model mouse is a useful animal for the evaluation of the photoprotective ability of sunscreens because photoresponses, even chronic changes, can be easily and quickly induced experimentally.

L4 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS
AU Tajima, Shingo
TI 12-O-Tetradecanoylphorbol 13-acetate (TPA)-induced reduction in **tropoelastin** expression is mediated by the activation of protein kinase C
SO Connect. Tissue (1997), 29(4), 235-240
CODEN: COTIE7; ISSN: 0916-572X
AB The addn. of 12-O-tetradecanoylphorbol 13-acetate (TPA) to quiescent

smooth muscle cell culture promoted cell **proliferation** and **inhibited** elastin expression simultaneously. We investigated the signal transduction pathways leading to the stimulation of cell proliferation and redn. in elastin expression by using various antagonists. The TPA-induced mitogenic effect was abolished by H-7, W-7 and heparin but not by HA1004, H-89 or tyrphostin. TPA-induced inhibition of elastin synthesis and its mRNA level were attenuated by H-7 or heparin but not by W-7, HA1004, H-89 or tyrphostin. The addn. of TPA to the quiescent cell culture resulted in the activation of protein kinase C which was abolished by H-7 or heparin but not by other antagonists. These results strongly suggest that the activation of protein kinase C is involved in TPA-induced cell proliferation and the redn. in elastin expression in vascular smooth muscle cells.

L4 ANSWER 6 OF 12 MEDLINE
AU Wachi H; Seyama Y; Tajima S
TI Modulation of elastin expression by heparin is dependent on the growth condition of vascular smooth muscle cells: up-regulation of elastin expression by heparin in the proliferating cells is mediated by the inhibition of protein kinase C activity.
SO JOURNAL OF BIOCHEMISTRY, (1995 Sep) 118 (3) 582-6.
Journal code: HIF; 0376600. ISSN: 0021-924X.
AB The effect of heparin on elastin expression in the proliferating and quiescent phases of growth of smooth muscle cells was studied. Heparin stimulated elastin synthesis and its mRNA level 2-3 fold in the proliferating cells while it **inhibited** the cell **proliferation**. The **inhibition** of cell **proliferation** and the stimulation of elastin expression by heparin in the proliferating cells were mimicked by a potent protein kinase C antagonist, H-7, but not by H-89, W-7, and HA1004, suggesting that the effect of heparin is mediated by the inhibition of protein kinase C. In contrast, heparin inhibited elastin synthesis and its mRNA level slightly but exhibited no effect on cell proliferation in the growth-arrested cells. This result indicates that heparin reciprocally affects elastin expression depending on the growth state of smooth muscle cells. Heparin thus exerts a complex influence on elastin expression in smooth muscle cells.

L4 ANSWER 7 OF 12 MEDLINE
AU Choi E T; Callow A D; Sehgal N L; Brown D M; Ryan U S
TI Halofuginone, a specific collagen type I inhibitor, reduces anastomotic intimal hyperplasia.
SO ARCHIVES OF SURGERY, (1995 Mar) 130 (3) 257-61.
Journal code: 8IA; 9716528. ISSN: 0004-0010.
AB OBJECTIVE: To determine if halofuginone hydrobromide, a specific type I collagen inhibitor, could prevent intimal hyperplasia at a vascular anastomosis. DESIGN: Intimal hyperplasia is characterized by smooth muscle cell proliferation and extracellular matrix accumulation. Halofuginone was used to block collagen production and smooth muscle cell proliferation in cell cultures and in a rabbit model of an end-to-end anastomosis of the right common carotid artery. Animals were fed a nontoxic dose of halofuginone. Eighteen rabbits were fed the inhibitor in a randomized blinded fashion and were examined after 4 weeks by harvesting the arteries after perfusion fixation at physiologic pressures. RESULTS: Halofuginone **inhibited** smooth muscle cell **proliferation** in vitro and

had no effect on cell viability. Morphometric quantification verified that halofuginone treatment significantly attenuated anastomotic intimal thickness. CONCLUSION: Oral administration of halofuginone inhibits intimal hyperplasia at vascular anastomoses. Intimal hyperplasia inhibition by halofuginone may be a therapeutic option for preventing arterial stenosis in vascular surgery.

L4 ANSWER 8 OF 12 MEDLINE
AU Hayashi A; Suzuki T; Wachi H; Tajima S; Nishikawa T; Murad S; Pinnell S R
TI Minoxidil stimulates elastin expression in aortic smooth muscle cells.
SO ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, (1994 Nov 15) 315 (1) 137-41.
Journal code: 6SK; 0372430. ISSN: 0003-9861.
AB Minoxidil was found to **inhibit** the **proliferation** of smooth muscle cells in the proliferating phase, but not in the quiescent phase. Treatment of proliferating or quiescent cells with minoxidil resulted in a dose- and time-dependent stimulation of elastin synthesis specifically. Maximum stimulation (fourfold) occurred in cells treated with 1 mM minoxidil for 48 h. The stimulation of elastin synthesis was accompanied by a proportional increase in elastin mRNA level, and it was partially prevented by a K+ channel blocker (tetraethylammonium) and completely prevented by high K+ salt (0.1 M). Minoxidil had no significant effect on the extent of prolyl hydroxylation in newly synthesized elastin. These results indicate that minoxidil stimulates elastin synthesis at a pretranslational level by a mechanism unrelated to cell proliferation but one that may involve K+ efflux. As a pharmacological agent capable of stimulating elastin expression, minoxidil would be a useful drug for the treatment of abnormal elastin metabolism.

L4 ANSWER 9 OF 12 MEDLINE DUPLICATE 3
AU Rabinovitch M
TI Investigational approaches to pulmonary hypertension.
SO TOXICOLOGIC PATHOLOGY, (1991) 19 (4 Pt 1) 458-69. Ref: 58
Journal code: TOY; 7905907. ISSN: 0192-6233.
AB Pulmonary vascular disease (PVD) revolves around a series of switches in the smooth muscle cell (SMC) phenotype. Differentiation of SMC from precursor cells causes muscularization of normally non-muscular peripheral arteries; hypertrophy and hyperplasia of existing SMC and increased connective tissue protein synthesis cause thickening of the wall, and migration of SMC into the subendothelial space is the basis of intimal proliferation. To uncover the pathophysiologic mechanisms of these changes, we have used a variety of animal models and cell culture systems. From rats in which hypertensive PVD was induced by exposure to chronic hypoxia or following injection of the pyrrolizidine alkaloid, monocrotaline, we have identified increased pulmonary artery (PA) elastolytic activity which occurs early and which accompanies progressive rather than reversible PVD. Inhibition of elastolytic activity prevents or reduces PVD. We are cloning the gene for this new enzyme to study its regulation in PVD. To address the mechanism of SMC proliferation under conditions of high PA pressure and flow, we cultured endothelial cells on polyvinylchloride membranes and pulsated them at high pressure. This caused reduced synthesis of heparan sulfate. The resulting decrease binding of fibroblast growth factor would lessen its mitogenic effect and modulate SMC proliferation in response to other growth factors from platelets or serum. To study SMC migration, we cultured endothelial and

SMC from the ductus arteriosus (a fetal vessel which spontaneously develops intimal proliferation in late gestation). The migratory SMC phenotype is a function of increased production of fibronectin governed by a translational control mechanism, and increased endothelial hyaluronan **regulated** by transforming growth factor beta. SMC **migration** is also related to impaired assembly of elastin, the result of a chondroitin sulfate-induced decrease in elastin binding proteins and the production of a novel 'defunct' 52 kD **tropoelastin**.

L4 ANSWER 10 OF 12 MEDLINE DUPLICATE 4
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TI [Changes in three-dimensional structure of the internal elastic membrane of rat aorta after its mechanical injury and regeneration]. Izmeneniia trekhmernoi struktury vnutrennei elasticheskoi membrany aorty krysy pri mekhanicheskom povrezhdenii i regeneratsii.
SO ARKHIV ANATOMII, GISTOLOGII I EMBRIOLOGII, (1991 Jan) 100 (1) 14-8.
Journal code: 8NS; 0370603. ISSN: 0004-1947.
AB By means of scanning electron microscopy of chemically extracted preparations the dynamics of changes in the three-dimensional structure of the internal elastic membrane (IEM) of the rat aorta has been investigated after its lesion by a vascular clip. The mechanical lesion results in rupture of the IEM along external borders of the instrument lips and in crushing of its central part. A niche is formed, along its periphery it is surrounded with a practically intact IEM. The aorta regeneration is accompanied with neoelastogenesis. In the center of the niche newly formed elastic structures appear later, but the IEM reparation develops more actively. During the neoelastogenesis some stages are distinguished: at first separate **elastic fibers** appear, which then anastomosed, uniting into fasciculi and laminae. It is supposed that the IEM-restoration at regeneration depends on synthetic activity of smooth myocytes and on the other hand, the changes in the IEM structure can **regulate** their **migration** and metabolism.

L4 ANSWER 11 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AU DAVIES J D; MERA S L
TI ELASTOSIS IN BREAST CARCINOMA II. ASSOCIATION OF PROTEASE INHIBITORS WITH IMMATURE **ELASTIC FIBERS**.
SO J PATHOL, (1987) 153 (4), 317-324.
CODEN: JPTLAS. ISSN: 0022-3417.
AB The elastosis of 11 invasive ductal and infiltrative lobular carcinomas of the breast was specifically immunostained for the plasma protease inhibitors alpha-1 antitrypsin, alpha-1 antichymotrypsin, alpha-2 macroglobulin, inter alpha trypsin inhibitor and C1 esterase inhibitor. None of these components was detected in the elastic fibres of normal ducts or blood vessels in the breast. The elastosis in breast carcinomas was also stained by Concanavalin A and Triticum vulgaris lectins. Such lectin staining probably represents binding to the microfibrillar component of elastic fibres, which is increased in immature elastic fibres, thus suggesting that the elastotic fibres of breast carcinoma are recently synthesised. It is suggested that the presence of protease inhibitors may influence the metabolism of elastic fibres, facilitating elastic fibre **proliferation** by the **inhibition** of elastinolytic enzymes.

L4 ANSWER 12 OF 12 MEDLINE DUPLICATE 5

AU Mecham R P; Lange G; Madaras J; Starcher B

TI Elastin synthesis by ligamentum nuchae fibroblasts: effects of culture conditions and extracellular matrix on elastin production.

SO JOURNAL OF CELL BIOLOGY, (1981 Aug) 90 (2) 332-8.
Journal code: HMV; 0375356. ISSN: 0021-9525.

AB Fetal bovine ligamentum nuchae fibroblasts maintained in culture synthesized soluble elastin but were unable to form the insoluble **elastic fiber**. Secreted elastin precursors accumulated in culture medium and were measured using a radioimmunoassay for elastin. When elastin production was examined in ligament tissue from fetal calves of various gestational ages, cells from tissue taken during the last trimester of development produced significantly more elastin than did cells from younger fetal tissue, with maximal elastin synthesis occurring shortly before birth. Soluble elastin was detected in ligament cells plated at low density until **proliferation** began to be density **inhibited** and the cells became quiescent. Also, soluble elastin production per cell declined with increasing population doubling or with age in culture. Cells grown in the presence of 5% fetal calf serum produced approximately four times as much soluble elastin as cells grown in serum-free medium. The addition of dexamethasone (0.1 microM) and bleomycin (1 microgram/ml) increased soluble elastin production by cultured cells 180% and 50%, respectively, whereas theophylline (5 micrograms/ml) depressed production 50% and antagonized stimulation by dexamethasone. Ascorbate (50 micrograms/ml), soybean trypsin inhibitor (1 mg/ml), insulin (100 microunits/ml), and aminoacetonitrile (50 micrograms/ml) had no effect, but cycloheximide at 10(-4) M completely inhibited soluble elastin production. In contrast to cells in culture, ligament tissue minces (ligament cells surrounded by in vivo extracellular matrix) efficiently incorporated soluble elastin precursors into insoluble, cross-linked elastin. In addition, soluble elastin production per cell (per microgram of DNA) was higher in tissue minces than elastin production by cells maintained on plastic. These results suggest a role for extracellular matrix in formation of the **elastic fiber** and in stabilizing elastin phenotypic expression by ligament fibroblasts. Fibroblasts from the bovine ligamentum nuchae present an excellent model for in vitro studies of elastin biosynthesis.

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L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 2000:608602 CAPLUS
DN 133:202978
TI Elastin-based compositions for screening of drugs for treatment of vascular diseases
IN Keating, Mark T.; Li, Dean Y.
PA University of Utah Research Foundation, USA
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000050068	A2	20000831	WO 2000-US2526	20000228
	WO 2000050068	A3	20011115		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1175225	A2	20020130	EP 2000-913319	20000228
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	US 1999-258217	A	19990226		
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